

modifications include the addition or "knock-in" of genes, and the removal or inactivation or "knock-out" of genes or their control sequences (Polejaeva *et al.*, Theriogenology, 53(1):117-26, 2000). Gene targeting techniques also promise the generation of transgenic animals in which specific genes coding for endogenous proteins have been replaced by human genes coding for exogenous human proteins. In 1993, Yom and Bremmel suggested that genes coding for major proteins in cow's milk could be replaced by human counterparts. Cows modified in this fashion would produce milk containing human milk proteins, which may be more nutritious for human infants and more suitable for infant formula manufacture (Yom, H.C. and Bremmel, R.D., American Journal of Clinical Nutrition, 1993, 58 (Supplement) 306S). Methods for producing exogenous proteins in the milk of pigs, sheep, goats and cows have been reported.--

Please replace the paragraph beginning at line 7 of page 28 with the following rewritten paragraph:

--In one embodiment of the instant invention, a nuclear donor cell is transfected with a vector construct that contains a transgene. Methods for transfection of somatic cell nuclei are well known in the art and include, by way of example, the use of retroviral vectors, retrotransposons, adenoviruses, adeno-associated viruses, naked DNA, lipid-mediated transfection, electroporation and direct injection into the nucleus. Such techniques, particularly as applied to avians, are disclosed in Bosselman (U.S. Patent No. 5,162,215), Etches (PCT Publication No. WO99/10505), Hodgson (U.S. Patent No. 6,027,722), Hughes (U.S. Patent No. 4,997,763), Ivarie (PCT Publication No. WO99/19472), MacArthur (PCT Publication No. WO97/47739), Perry (U.S. Patent No. 5,011,780), Petitte (U.S. Patent Nos. 5,340,740 and 5,656,479), and Simkiss (PCT Publication No. WO90/11355), the disclosures of which are incorporated by reference herein.--

//

//

Please replace the paragraph beginning at line 1 of page 30 with the following rewritten paragraph:

Q3
--In another embodiment of the instant invention, a knock-in animal has been manipulated such that it carries a specific nucleic acid sequence such as a "knock-in sequence" in a predetermined coding or noncoding region of its genome. The knock-in sequence may replace all or part of an endogenous gene of the animal by a functional homologous gene or gene segment of another animal. Knock-in animals can be prepared according to a variation of the standard knock-out method, comprising the introduction of a foreign gene into the targeting vector, in such a way that the introduced gene would be under the control of the regulatory elements that normally control the expression of the endogenous gene (Le Mouellic *et al.*, *Proc. Natl. Acad. Sci. USA* 87:4712-6, 1990) and (McCreath *et al.*, *Nature* 405:1066-1069, 2000).--

Please replace the paragraph beginning at line 16 of page 31 with the following rewritten paragraph:

Q4
--Ova were isolated from euthanized hens between 2-4 hours after oviposition of the previous egg. Alternatively, eggs were isolated from hens whose oviducts have been fistulated (Gilbert and Woodgush, *Journal of Reproduction and Fertility* 5:451-453, 1963) and (Pancer *et al.* *Br. Poult. Sci.* 30:953-7, 1989).--

//
//
//
//
//
//
//
//
//
//